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Original Research Article

## Colposcopic evaluation of cervix with abnormal papsmear findings: prospective analytical study at our tertiary care centre

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### ABSTRACT

**Background:** Pap test has been successful in reducing the incidence of cervical cancer by 80% and mortality by 70%. Any women with a cytologic specimen suggesting the presence of HSIL on Pap smear should undergo colposcopy and dissected biopsy. Prevention of invasive cancer by early detection and treatment of cervical intraepithelial neoplasia (CIN) currently offers the most cost effective, long term strategy for cervical cancer control. The aim of study was to minimise disagreements and make colposcopy assessment quick, accurate and easy for follow-up.

**Methods:** Prospective analytical study of 300 gynaecological patients with abnormal Pap smear findings between June 2020 to Dec 2020 at R.N.T. Medical College, Udaipur. All of them were subjected to colposcopy and dissected biopsy from the abnormal areas. The incidence of CIN/invasive carcinoma was calculated by proportion/percentage.

**Results:** Incidence of invasive carcinoma was <1% but the incidence of premalignant lesion CIN was high (20.9%), CIN 2/3 and CIS were present in 6.9%.

**Conclusions:** Patients with persistent inflammation pap smear can harbour high proportion of CIN and hence these patients need further evaluation through colposcopy.

**Keywords:** Colposcopy cervical intraepithelial neoplasia, Invasive cancer, Reid colposcopy index

### INTRODUCTION

Chronic inflammation, either specific or non-specific, has been shown to be associated with malignancy and was thought to be one of the factors responsible for carcinogenesis. Persistent inflammation leads to increased cellular turnover, especially in the epithelium, and provides a selection pressure that results in the emergence of cells that are at a high risk for malignant transformation.<sup>1</sup> Inflammatory Pap smear is the most common report the gynecologist receives even when the cervix appears normal. The original Papanicolaou classification of class 2 smears denotes inflammation and the recommendation is to repeat the smear after treating the infection.<sup>2</sup> However, this does not specify the type of infection and the presenting of Pap smear by the

Bethesda system reports on specific infections and classifies it under benign cellular changes.<sup>3</sup> The cervical screening algorithm for benign cellular changes recommends treatment of infection if indicated and performing a repeat Pap smear in 4 to 6 months time and if the inflammatory changes persist, to subject the patient to colposcopy.<sup>4</sup>

In practice, however, this is not always followed, especially in developing countries. The significance of cervical cytology with atypia has been extensively studied. There is a great controversy regarding the optimal management of women with persistent inflammatory changes without atypia, some considering it less likely to be associated with dysplasia and others recommending further evaluation as it is associated with

a high incidence of cervical intraepithelial neoplasia (CIN).<sup>5-7</sup>

Hence, we have undertaken this study with the objectives to study the colposcopic features in the cervix of persistent inflammatory cellular changes on Pap smear, to study epithelial cell abnormalities by colposcopic biopsy of abnormal areas in such cases and to determine the existence of significant cervical intraepithelial lesions or invasive carcinoma in patients with persistent inflammatory Pap smear.

## METHODS

This is a prospective analytical study conducted in the Department of Obstetrics and Gynecology, RNT Medical College, Udaipur between August 2006 and June 2008.

One hundred and fifty women who showed persistent inflammatory changes on Pap smear were included in the study.

Patients with persistent inflammatory changes with atypical dysplastic cells, patients with Diabetes mellitus, pregnant women and patients with previous cervical surgery were excluded. The study was approved by the Institute Scientific and Ethical Committee.

Patients with a report of inflammatory Pap smear were selected at random for initial recruitment. These patients were advised to use clotrimazole or betadine vaginal pessaries for a minimum of 6 days. Those with a clinical diagnosis of chronic pelvic inflammatory disease and showing inflammatory Pap smear were given Doxycycline and Metronidazole for a minimum period of 14 days along with vaginal pessaries.

A repeat Pap smear was performed after a period of 2 weeks with Ayer's wooden spatula. No preparation of the cervix was undertaken at the time of sampling and women were not menstruating or using any vaginal douche or vaginal contraceptives at the time of sampling. If inflammatory cellular changes were reported again on the repeat Pap smear, these patients were subjected to colposcopic examination after taking informed consent.

The woman was kept in a dorsal position and the cervix was exposed by inserting a Cusco's speculum. Excess mucus was wiped off with a cotton swab soaked in saline. Five percent acetic acid was applied to the cervix and it was visualized using a binocular colposcope (M/s Olympus Optical Co. Ltd., Tokyo, Japan) under 40X magnification. Biopsies were taken from the abnormal areas (aceto white areas and vascular abnormalities like fine punctuations, coarse punctuations, mosaic and areas 1/11/2021 colposcopic evaluation of cervix with persistent inflammatory Pap smear: A prospective analytical study showing atypical vasculature) and an endo cervical curettage was performed. All the specimens were subjected to histopathological examination. The

incidence of pre-malignant and malignant lesions was calculated as percentages.

## RESULTS

The mean age was 37 years and the mean parity was 2.6. The most common symptom was vaginal discharge followed by pelvic pain and in 45% of the patients the clinical diagnosis was pelvic inflammatory disease. Abnormal uterine bleeding and erosion of the cervix also contributed to inflammatory smear in approximately 20% of the patients (Table 1).

**Table 1: Clinical profile.**

Clinical characteristic	Number	Percentage
Mean age	37 years	
Mean parity	2.6	
<b>Symptomatology</b>		
White discharge per vaginam	134	44.7
Pelvic pain	82	27.3
AUB	36	12
Post-coital bleeding	18	6
Mass descending per vaginam	12	4
Post-menopausal bleeding	10	3.3
Dysmenorrhea	8	2.7
<b>Clinical diagnosis</b>		
PID	104	34.7
AUB	64	21.3
Cervix erosion	62	20.7
Unhealthy cervix	40	13.3
Uterovaginal prolapsed	12	4
Ovarian cyst	10	3.3
Fibroid uterus	8	2.7

The colposcopic features of patients with persistent inflammatory pap smears (Table 2). The most common feature was aceto whiteness (41.3%) followed by a combination of aceto whiteness and vascular abnormality (24.7%). Colposcopy was normal in nine patients and hence no biopsy was taken. Erosion was confirmed by colposcopy in 12% of the patients. Biopsy was also not performed when the margins of erosion were regular and these accounted for five cases.

The correlation of inflammatory Pap smear with colposcopic biopsy results (Table 3). The most common biopsy result in patients with inflammatory pap smear was chronic cervicitis (28.7%). Human papilloma virus (HPV) lesions accounted for 21.2% CIN 1 for 14.7% and CIN 2/3 for 4.4% of the cases. The two cases of carcinoma in situ and one case of invasive carcinoma also showed non-specific inflammation on Pap test. Ten percent (14/150) did not require biopsy.

**Table 2: Colposcopic features of patients with inflammatory Pap smear.**

Inflammatory Pap smear	Normal	Erosion	Acetowhite areas	Vascular abnormalities	Acetowhite areas and vascular abnormalities
<b>Non-specific inflammation (n=276)</b>	14 (5.07)	36 (13.04)	106 (38.40)	51 (18.47)	69 (25)
<b>Bacterial vaginosis (n=12)</b>	2	-	2	2	6
<b>Candida albicans (n=6)</b>	2	-	2	-	2
<b>Trichomonas vaginalis (n=6)</b>	-	-	4	-	2
<b>Total (n = 300)</b>	18 (6)	36 (12)	114 (38)	53 (17.66)	79 (26.33)

**Table 3: Correlation of inflammatory Pap smear with colposcopic biopsy.**

Persistent inflammatory Pap smear (Cytodiagnosis)	No biopsy	Normal tissue	SM	Chronic cervicitis (CC)	SM +CC	HPV lesions	CIN1	CIN2	Cain situ	Invasive Ca
<b>Non-specific inflammation (n=276-24) (252)</b>	24	34 (14)	4 (2)	70 (28)	34 (14)	58 (23)	36 (15)	10 (4)	4 (2)	2 (0.7)
<b>Bacterial vaginosis (n=8)</b>	2	2		4			2	2		
<b>Candida albicans (n=6)</b>	2	2								
<b>Trichomonas vaginalis (n=3)</b>				2	2		2			
<b>Total biopsies (300-28) (n=272)</b>	28	38 (13.9)	4 (1.5)	78 (28.7)	36 (13.2)	58 (21.2)	40 (14.7)	12 (4.4)	4 (1.5)	2 (0.7)

**Table 4: Correlation of clinical symptoms and colposcopic findings.**

Clinical symptom	Colposcopic findings					Total
	Normal	Erosion	Acetowhite areas(AW)	Vascular abnormality(VA)	AW +VA	
<b>Vaginal discharge(n=134)</b>	6	26	46 (34)	18	38 (28)	134
<b>Pelvic pain (n=82)</b>	6	6	38 (46)	12	20 (24)	82
<b>AUB (n =18)</b>	2	-	14	14	6	36
<b>Post-coital bleeding (n =18)</b>	-	4	8	-	6	18
<b>Mass per vaginum (n =12)</b>	-	-	6	4	2	12
<b>Post-menopausal bleeding(n=10)</b>	-	-	6	2	2	10
<b>Dysmennorrhea (n =8)</b>	4	-	4	-	-	8
<b>Total (n =300)</b>	18 (6)	36 (12)	122 (40.7)	50 (16.7)	74 (24.7)	300

The correlation between clinical symptomatology and colposcopic features (Table 4). The most common colposcopic feature is aceto whiteness followed by a combination of acetowhite areas and vascular abnormality, irrespective of the symptoms. Of the patients who presented with pelvic pain, 46% showed ace to white areas and 24% showed a combination of ace to

white areas and vascular abnormality. This is slightly higher than the patients presenting with vaginal discharge per vaginum who showed ace to white areas in 34% of the cases and a combination of acetowhite areas and vascular abnormality in 28% of the cases. Erosion was more common in patients with vaginal discharge than in those with pelvic pain.

The results of colposcopic biopsy in correlation with symptomatology (Table 5). The patient with invasive carcinoma presented with pelvic pain and two patients with carcinoma in situ presented with post-coital bleeding. In patients who presented with vaginal discharge, the most common diagnosis was chronic cervicitis followed by HPV lesions in 17% and CIN 1 in another 17% of the cases. Patients with abnormal uterine bleeding also showed a significantly increased incidence of CIN (22.2%).

Of the benign lesions, chronic cervicitis and HPV changes were common. Acanthosis, koilocytosis, chronic cervicitis with koilocytosis, squamous metaplasia with koilocytosis, acanthosis with koilocytosis and koilocytic atypia were grouped under HPV changes. The incidence of invasive carcinoma was <1%. But, the incidence of pre-malignant lesions was high (20.9%). CIN 2/3 and carcinoma in situ together contributed to 6.9% of the cases.

**Table 5: Clinical symptoms and colposcopic biopsy results.**

Colposcopic biopsy histopathological examination results										
Clinical symptoms	No biopsy	Normal tissue	Squamous metaplasia (SM)	Chronic cervicitis (CC)	SM+CC	HPV lesions	CIN1	CIN2	CIN3	Invasion
Vaginal discharge (n=124)	16	24	2	34	6	24	24 (17.9)	4 (2.9)	-	-
Pelvic pain (n=82)	6	10	-	18	22	16	6 (7.3)	2 (2.4)	-	2 (2.4)
AUB (n=36)	4	4	-	16	-	6	6 (16.7)	2 (5.6)	-	-
Post-coital bleeding (n=18)	-	-	-	6	2	4	2	-	4 (22)	-
Mass per vaginum (n=12)	-	-	-	2	4	6	-	-	-	-
Post-menopausal bleeding (n=10)	-	-	-	2	2	-	2	4	-	-
Dysmenorrhoea (n=8)	4	-	2	-	-	2	-	-	-	-
<b>Total (n=300)</b>	<b>28 (9.3)</b>	<b>38 (12.7)</b>	<b>4 (1.3)</b>	<b>78 (26)</b>	<b>36 (12)</b>	<b>58 (19.3)</b>	<b>40 (13.3)</b>	<b>12 (4)</b>	<b>4 (1.3)</b>	<b>2 (0.7)</b>

## DISCUSSION

Cervical cancer screening was proved to be an important part of preventive health care of women. Attempts are being made to improve the efficacy of the screening programme to decrease the morbidity and mortality due to cervical cancer. The cervical screening algorithm for benign cellular changes on Papsmear recommends treatment of infection if indicated and a repeat Pap smear in 4-6 months time, and, if the inflammatory changes still persist, to subject the patient to colposcopy. However, in practice, this is not followed, especially in developing countries like ours, where proper screening protocols are not available/ followed. Hence, a good number of patients in the pre-malignant stage are being missed.

Obstetrician Gynecologists do not review the Pap smear result with the cytologists and 41% do nothing when

inflammatory Pap smear is reported. Only 11% treat the infection and repeat Pap smear and 24% treat infection and do not repeat Pap smear.

There are very few studies in the literature where the incidence of premalignant and malignant lesions was looked into in cases of inflammatory Pap smear. Inflammation can obscure few malignant cells and may result in high false negative rates and the same may be reduced by employing liquid based cytology.<sup>8</sup> However, it was reported that liquid based cytology was not cost-effective for developing countries and the recent studies did not report a statistically significant difference of accuracy between conventional Pap test and liquid based cytology.<sup>9</sup> The main reason for false-negative reports of cytology were found to be sampling errors, with sampling errors as high as 42.5% being suboptimal and 17.5% being inadequate for interpretation.<sup>10</sup> Mc Lachlan et al studied the colposcopic features and biopsy results of 102

women with persistent inflammatory Pap smears and found 19% cases of CIN 2 or worse.<sup>11</sup> This is almost similar to the present study.

The mean age and parity in the present study was higher (37 years and 2.6) than that of Seckin et al, where the mean age was 30.2 years and the parity was 1.7. The most common persistent inflammatory Pap smear subjected to colposcopy was presumed to be non-specific in the study of Seckin et al, as they did not specify on the type of inflammatory smear.<sup>6</sup>

In the present study, 92% were non-specific inflammation and only 8% were specific inflammation due to *Trichomonas vaginalis*, *Candida albicans* and *bacterial vaginosis*. Wilson et al included bacteriological cultures of cervico vaginal smears to diagnose specific infections and found an increased incidence of sexually transmitted infections in patients <25 years of age and in many showing abnormal colposcopic features in this age group.<sup>7</sup> Colposcopy was normal in 9.3% of the patients in the present study, which was much lower than that of Seckin et al, who reported 29.1% to be normal. A very high percentage (62.5%) of normal colposcopic findings was reported by Wilson et al in 96 patients of inflammatory Pap smears. This is in contrast with the results of the present study.

Colposcopic biopsy showed benign lesions in 48.2% of the cases in the study done by Seckin et al, which was lower than that reported in the present study. Seckin reported a very high incidence of HPV-related lesions (64.5%) where as Frisch reported an incidence of only 8%.<sup>12</sup> HPV related lesions constituted only 19.4% in the present study. The incidence of pre-malignant lesions in the present study (20.9%) was closer to that of Frisch (23.5%) but much higher than that of Seckin et al (8%-18 out of 224). There were no cases of malignancy in the series of Seckin and Frisch but in the present study, one case was found. Recently, Hammes et al evaluated the population of macrophages during the cervical malignant transformation and its influence on CIN in cervical biopsy specimens. They concluded that macrophage count and inflammation increased linearly with disease progression. Inflammation was present in 25%, 46.1%, 58.4% and 89.3% of normal, Low grade squamous intraepithelial lesion (LGSIL), (High grade squamous intraepithelial lesion) HGSIL and squamous cell carcinoma, respectively.<sup>13</sup>

Seckin recommends colposcopic evaluation of patients with persistent inflammatory Pap smear despite therapy in any population in any part of the World. Frisch is of the opinion that colposcopy of women with cytologic diagnosis of inflammatory epithelial changes may be a useful way to detect otherwise unrecognized cases of CIN, and the present study highlights these statements.

## CONCLUSION

Patients with persistent inflammatory Pap smears can harbour a high proportion of CIN and HPV infection and hence these patients will need further evaluation by colposcopy.

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